

Appl. No. : 07/817,014
Filed : March 23, 2001

sequence specific of said microorganisms of family type discriminated from homologous sequences upon any type of microarrays or biochips by any method.

Please replace the paragraphs beginning on page 21, line 5 through page 21, line 30, with the following rewritten paragraphs:

S. aureus 1 : 5' CTTTGCTGATCGTGATGACAAA 3' (SEQ ID NO: 1)
S. aureus 2 : 5' TTTATTAAAATATCACGCTCTCG 3' (SEQ ID NO: 2)
S. epidermidis 1 : 5' TCGCGGTCCAGTAATAGATTATA 3' (SEQ ID NO: 3)
S. epidermidis 2 : 5' TGCATTCCAGTTATTCTCCC 3' (SEQ ID NO: 4)
S. haemolyticus 1 : 5' ATTGATCATGGTATTGATAGATAC 3' (SEQ ID NO: 5)
S. haemolyticus 2 : 5' TTTAATCTTTGAGTGTCTTATAC 3' (SEQ ID NO: 6)
S. saprophyticus 1 : 5' TAAAATGAAACAACCGGTTATAAG 3' (SEQ ID NO: 7)
S. saprophyticus 2 : 5' AAACTATCCATACCATTAAAGTACG 3' (SEQ ID NO: 8)
S. hominis 1 : 5' CGACCAGATAACAAAAAAGCACAA 3' (SEQ ID NO: 9)
S. hominis 2 : 5' GTAATCGTTACCATGTTCTAA 3' (SEQ ID NO: 10)

The PCR was performed in a final volume of 50 µl containing: 1.5 mM MgCl₂, 10 mM Tris pH 8.4, 50 mM KCl, 0.8 µM of each primer, 50 µM of each dNTP, 50 µM of biotin-16-dUTP), 1.5 U of Taq DNA polymerase Biools, 7.5% DMSO, 5 ng of plasmid containing *FemA* gene. Samples were first denatured at 94 °C for 3 min. Then 40 cycles of amplification were performed consisting of 30 sec at 94 °C, 30 sec at 60 °C and 30 sec at 72 °C and a final extension step of 10 min at 72 °C. Water controls were used as negative controls of the amplification. The sizes of the amplicons obtained using these primers were 108 bp for *S. saprophyticus*, 139 bp for *S. aureus*, 118 bp for *S. hominis*, 101 bp for *S. epidermidis* and 128 bp for *S. haemolyticus*. The sequences of the capture nucleotide sequences were the same as the corresponding amplicons but they were single strands.

Appl. No. : 09/817,014
Filed : March 23, 2001

Please replace the table on page 24, beginning at line 1, with the following rewritten table:

Name	Sequence (5' -> 3')
Capture nucleotide sequence	
ATaur02	ATTTAAAATATCACGCTCTCGTTAG (SEQ ID NO: 11)
ATepi02	ATTAAGCACATTCTTCATTATTTAG (SEQ ID NO: 12)
AThae02	ATTTAAAGTTCACGTTCATTGTAA (SEQ ID NO: 13)
ATHom02	ATTTAATGTCTGACGTTCTGCATGAAG (SEQ ID NO: 14)
ATsap02	ACTTAATACTCGCGTTCAGCCTTAA (SEQ ID NO: 15)

Please replace the paragraphs on page 24, lines 7-9, with the following rewritten paragraphs:

APstap03: 5' CCCACTCGCTTATATAGAATTGA 3' (SEQ ID NO: 16)

APstap04: 5' CCACTAGCGTACATCAATTGA 3' (SEQ ID NO: 17)

APstap05: 5' GGTTTAATAAGTCACCAACATATT 3' (SEQ ID NO: 18)

Please replace the table on page 25, beginning at line 13, with the following table:

Name	Sequence (5' -> 3')
Capture nucleotide sequence	
Ataur02	ATTTAAAATATCACGCTCTCGTTAG (SEQ ID NO: 11)
ATepi02	ATTAAGCACATTCTTCATTATTTAG (SEQ ID NO: 12)
ATepi03	<u>GAATTCAAAGTTGCTGAGAA</u> ATTAAGCACATTCTTC ATTATTTAG (SEQ ID NO: 19)

Appl. No. : 69817,014
Filed : March 23, 2001

ATepi04	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGATTAAGCACATTCTTCATTATTTAG</u> (SEQ ID NO: 20)
ATepi05	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGTCTTCTTAAAATCTAAAGAAATTAAAGCACATTCTT</u> CATTATTTAG (SEQ ID NO: 21)

^aThe spacer sequences are underlined

Please replace the table on page 26, beginning at line 12, with the following table:

Name	Sequence (5' -> 3')
Capture nucleotide sequence	
Ataur27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG</u> ATTAAAATATCACGCTCTCGTTAG (SEQ ID NO: 22)
Atepi27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG</u> ATTAAGCACATTCTTCATTATTTAG (SEQ ID NO: 23)
Athae27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG</u> ATTAAAGTTCACGTTCATTTGTAA (SEQ ID NO: 24)
Athom27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG</u> ATTTAATGTCTGACGTTCTGCATGAAG (SEQ ID NO: 25)
Atsap27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG</u> ACTTAATACTTCGCGTTCAGCCTTAA (SEQ ID NO: 26)

^aThe spacer sequence is underlined. The specific sequences were of 27 bases

Appl. No. : 09/817,014
Filed : March 23, 2001

Please replace the paragraphs on page 27, lines 6-7, with the following rewritten paragraphs:

APcons3-1: 5' TAAYAAARTCACCAACATAYTC 3' (SEQ ID NO: 27)

APcons3-2: 5' TYMGNTCATTATGGAAGATAC 3' (SEQ ID NO: 28)

Please replace the tables and paragraphs beginning on page 28, line 4, through page 41, line 19, with the following rewritten tables and paragraphs:

Name	Sequence (5' -> 3')
Capture nucleotide sequence	
Ataur15	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGTCTTCTTAAAATGCTCTCGTTAGTT</u> (SEQ ID NO: 29)
Ataur27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGATTAAAATATCGCTCTCGTTAG</u> (SEQ ID NO: 22)
Ataur40	<u>GAATTCAAAGTTGCTGAGAATAGTTCAAATCTTATTAA</u> <u>AAATATCACGCTCTCGTTAGTTCTT</u> (SEQ ID NO: 30)
Atana15	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGTCTTCTTAAAATGCTCTTCATTAGTT</u> (SEQ ID NO: 31)
Atana27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGGTTAAAATATCACGCTCTCATTAG</u> (SEQ ID NO: 32)
Atana40	<u>GAATTCAAAGTTGCTGAGAATAGTTCAAATCTTGTAA</u> <u>AAATATCACGCTCTCATTAGTTCTT</u> (SEQ ID NO: 33)

Appl. No. : 09/817,014
Filed : March 23, 2001

Atepi15	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGTCTTCTTAAAATTTCATTATTTAGTT</u> (SEQ ID NO: 34)
Atepi27	<u>GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAG</u> <u>CGATTAAGCACATTCTTCATTATTTAG</u> (SEQ ID NO: 23)
Atepi40	<u>GAATTCAAAGTTGCTGAGAATAGTTCAAATCTTATTAA</u> <u>GCACATTCTTCATTATTTAGTTCCCTC</u> (SEQ ID NO: 35)

Example 6: Sensitivity of the detection of FemA sequences of *Staphylococcus aureus* on arrays bearing specific sequence as proposed by this invention and the consensus sequence (figure 4)

The experiment was conducted as described in example 4 with the capture nucleotide sequences spotted at concentrations of 3000 nM. The bacterial FemA sequences were serially diluted before the PCR and being incubated with the arrays.

Example 7: Detection of 16 homologous FemA sequences on array

The consensus primers and the amplicons were the same as described in the example 4 but the capture probes were chosen for the identification of 15 Staphylococcus species. The experiment is conducted as in example 4. The capture probes contain a spacer fixed on the support by its 5' end and of the following sequence 5'

GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ ID NO: 36)
followed by the following specific sequences for the various femA from the different Staphylococcus.

Appl. No. : 09/817,014
Filed : March 23, 2001

S. aureus ATTTAAAATATCACGCTCTCGTTAG (SEQ ID NO: 37)
S. epidermidis ATTAAGCACATTCTTCATTATTTAG (SEQ ID NO: 38)
S. haemolyticus ATTTAAAGTTCACGTTCATTTGTAA (SEQ ID NO: 39)
S. hominis ATTTAATGTCTGACGTTCTGCATGAAG (SEQ ID NO: 40)
S. saprophyticus ACTTAATACTCGCGTCAGCCTTAA (SEQ ID NO: 41)

S. capitis ATTAAGAACATCTCTTCATTATTAAG (SEQ ID NO: 42)
S. caseolyticus ATAAAGACATTCGAGACGAAGGCT (SEQ ID NO: 43)
S. cohnii ACTTAACACTTCACGCTCTGACTTGAG (SEQ ID NO: 44)
S. gallinarum ACTTAAAACCTCACGTTCAGCAGTAAG (SEQ ID NO: 45)
S. intermedius GTGGAAATCTTGCTCTTCAGATTCAG (SEQ ID NO: 46)
S. lugdunensis TTCTAAAGTTGTCGTTCATTCGTTAG (SEQ ID NO: 47)
S. schleiferi TTTAAAGTCTTGCCTTCAGTGTGAG (SEQ ID NO: 48)
S. sciuri GTTGTATTGTTCATGTTCTTTCTAA (SEQ ID NO: 49)
S. simulans TTCTAAATTCTTGTTCAGCGTTCAA (SEQ ID NO: 50)
S. warneri AGTTAAGGTTCTTTTCATTATTGAG (SEQ ID NO: 51)
S. xylosus GCTAACACCTCACGTTGAGCTGCAA (SEQ ID NO: 52)

Example 8: Detection of 19 homogous p34 Sequences of Mycobacteria

The P34 genes present in all *Mycobacteria* are all amplified with the following consensus primers

Sense

MycU4 5' CATGCAGTGAATTAGAACGT 3' (SEQ ID NO: 53) located at the position 496-515 of the gene, Tm = 56°C

Appl. No. : 09/817,014
Filed : March 23, 2001

Antisense

APmcon02 5' GTASGTCATRRSTYCTCC 3' (SEQ ID NO: 54) located at the position position 733-750 of the gene, Tm = 52-58°C

S = C or G

R = A or G

Y = T or C

The size of amplified products ranges from 123 to 258 bp

The following capture probes have been chosen for the specific capture of the Mycobacteria sequences.

Capture probes

Avium :	5' CGGTCGTCTCCGAAGCCCCGCG 3' (21 nt) (SEQ ID NO: 55)
Gastrii 1 :	5' GATCGGCAGCGGTGCCGGGG 3' (20 nt) (SEQ ID NO: 56)
Gastrii 3 :	5' GTATCGCGGGCGGCAAGGT 3' (19 nt) (SEQ ID NO: 57)
Gastrii 5 :	5' TCTGCCGATCGCAGCGGTGCCGG 3' (24nt) (SEQ ID NO: 58)
Gastrii 7 :	5' GCCGGGGCCGGTATCGCGGGCGG 3' (24nt) (SEQ ID NO: 59)
Gordonae :	5' GACGGGCACTAGTTGTCAGAGG 3' (22 nt) (SEQ ID NO: 60)
Intracellularare 1:	5' GGGCCGCCGGGGCCTCGCCG 3' (21 nt) (SEQ ID NO: 61)
Intracellularare 3 :	5' GCCTCGCCGCCAAGACAGTG 3' (21 nt) (SEQ ID NO: 62)
Leprae:	5' GATTTCGGCGTCCATCGGTGGT 3' (22 nt) (SEQ ID NO: 63)
Kansasi 1 :	5' GATCGTCGGCAGTGGTGACGG 3' (21 nt) (SEQ ID NO: 64)
Kansasi 3 :	5' TCGTCGGCAGTGGTGAC 3' (17 nt) (SEQ ID NO: 65)
Kansasi 5 :	5' ATCCGCCGATCGTCGGCAGTGGTGACG 3' (27 nt) (SEQ ID NO: 66)
Malmoense :	5' GACCCACAACACTGGTCGGCG 3' (21 nt) (SEQ ID NO: 67)
Marinum :	5' CGGAGGTGATGGCGCTGGTCG 3' (21 nt) (SEQ ID NO: 68)
Scrofulaceum :	5' CGGCAGCACGGATCGCGTC (20 nt) (SEQ ID NO: 69)
Simiae:	5' ATCGCTCCTGGTCGCGCCTA 3' (20 nt) (SEQ ID NO: 70)

Appl. No. : 09/817,014
Filed : March 23, 2001

Szulgai : 5' CCCGGCGCGACCAGCAGAACG 3' (21 nt) (SEQ ID NO: 71)
Tuberculosis: 5' GCCGTCCAGTCGTTAATGTCGC 3' (22 nt) (SEQ ID NO: 72)
Xenopi: 5' CGGTAGAAGCTGCGATGACACG 3' (22 nt) (SEQ ID NO: 73)

Each of the sequences above comprises a spacer at its 5' end
Spacer sequence 5' GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ
ID NO: 36). Capture probes are aminated at their 5' end.

Example 9: Detection of *MAGE* genes

MAGE genes are all amplified with the following consensus primers

Sense

- DPSCONS2 5' GGGCTCCAGCAGCCAAGAAAGAGGA 3' (SEQ ID NO: 74), located at the
398-421 position of the gene

Tm = 78°C

Other amplicons have been added as sense primer in order to increase the efficiency of
the PCR for some *MAGE*s

- DPSMAGE1 5' GGGTTCCAGCAGCCGTGAAGAGGA 3' (SEQ ID NO: 75)

Tm = 78°C

- DPSMAG8 5' GGGTTCCAGCAGCAATGAAGAGGA 3' (SEQ ID NO: 76) Tm = 74°C

- DPSMAG12 5' GGGCTCCAGCAACGAAGAACAGGA 3' (SEQ ID NO: 77)

Tm = 76°C

Antisense

- DPASCONB4 5' CGGTACTCCAGGTAGTTTCCTGC 3' (SEQ ID NO: 78), located at the
position 913-936 of the gene, Tm = 74°C

The size of the amplified products is around 530 bp

The following capture probes of 27 nucleotides have been chosen for the specific capture
of the *MAGE* sequences.

Appl. No. : 09/817,014
Filed : March 23, 2001

Capture probes

Mage 1 DTAS01 5'	ACAAGGACTCCAGGATACAAGAGGTGC 3' (SEQ ID NO: 79)
Mage 2 DTAS02 5'	ACTCGGACTCCAGGTCGGAACATTG 3' (SEQ ID NO: 80)
Mage 3 DTS0306 5'	AAGACAGTATCTTGGGGATCCCAAGA 3' (SEQ ID NO: 81)
Mage 4 DTAS04 5'	TCGGAACAAGGACTCTGCGTCAGGCGA 3' (SEQ ID NO: 82)
Mage 5 DTAS05 5'	GCTCGGAACACAGACTCTGGGTCAAGGG 3' (SEQ ID NO: 83)
Mage 6 DTS06 5'	CAAGACAGGCTTCCTGATAATCATCCT 3' (SEQ ID NO: 84)
Mage 7 DTAS07 5'	AGGACGCCAGGTGAGCGGGGTGTCT 3' (SEQ ID NO: 85)
Mage 8 DTAS08 5'	GGGACTCCAGGTGAGCTGGGTCCGGGG 3' (SEQ ID NO: 86)
Mage 9 DTAS09 5'	TGAACCTCAGCTGAGCTGGTCGACCG 3' (SEQ ID NO: 87)
Mage 10 DTAS10 5'	TGGGTAAAGACTCACTGTCTGGCAGGA 3' (SEQ ID NO: 88)
Mage 11 DTAS11 5'	GAAAAGGACTCAGGGTCTATCAGGTCA 3' (SEQ ID NO: 89)
Mage 12 DTAS12 5'	GTGCTACTTCCAAGCTCGTCTCCAGGT 3' (SEQ ID NO: 90)

Each of the sequences above comprises a spacer aminated at its 5' end in order to be covalently linked to the glass

Spacer sequence 5' GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ ID NO: 36)

They are spotted on aldehyde bearing glasses and used for the detection of the MAGEs amplified by the consensus primers given here above. The results show a non equivocal identification of the MAGEs present in the tumors compared to identification using 12 specific PCR, one for each MAGE sequences.

Example 10: Identification of G-protein dopamine receptors subtypes in rat

Dopamine Receptor coupled to the G-protein are all amplified with the following consensus primers

Sense

- CONSENSUS2-3-4

Appl. No. : 09/817,014
Filed : March 23, 2001

5' TGCAGACM~~A~~CCACCAACTACTT 3' (SEQ ID NO: 91) located at the position 221-242 of the gene, Tm = 66°C

M = A or C

- CONSENSUS1-5

5' TGMGGKCCAAGATGACCAACWT 3' (SEQ ID NO: 92) (22 nt) located at the position 221-240 of the gene, Tm = 66°C

M = A or C

K = G or T

W = A or T

Antisense

5' TCATGR~~C~~R~~C~~SAGGTT~~C~~AGGAT 3' (SEQ ID NO: 93) located at the position 395-416 of the gene, Tm = 64-68°C

R = A or G

S = C or G

The size of the amplified product is 196 bp.

The following capture probes of 27 nucleotides have been chosen for the specific capture of the dopamine receptor sequences.

Capture probes

DRD1 5' CTGGCTTTGGC~~T~~GGGTCC~~T~~TT 3' (SEQ ID NO: 94)

DRD2 5' TGATTGGAAATT~~C~~AGCAGGATTCACTG 3' (SEQ ID NO: 95)

DRD3 5' GAGTCTGGAATT~~C~~AGCCGCATTGCT 3' (SEQ ID NO: 96)

DRD4 5' CGTCTGGCTGCTGAGCCCCCGCCTCTG 3' (SEQ ID NO: 97)

DRD5 5' CTGGGTACTGCC~~T~~GGGACATTCT 3' (SEQ ID NO: 98)

Each of the sequences above comprises an aminated spacer at its 5' end. Spacer sequence 5' GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG (SEQ ID NO: 36)

Appl. No. : 09/817,014
Filed : March 23, 2001

Example 11: Identification of G-protein histamine receptors subtypes in rat

Histamin Receptor coupled to the G-protein are all amplified with the following primers

Sense

- H1sense

5' CTCCGTCCAGCAACCCCT 3' (SEQ ID NO: 99) (18 nt) located at the Position 381-398 of the gene, Tm = 60°C

- H2sense

5' CTGTGCTGGTCACCCCAGT 3' (SEQ ID NO: 100) (19 nt) located at the Position 380-398 of the gene, Tm = 62°C

- H3sense

5' ACTCATCAGCTATGACCGATT 3' (SEQ ID NO: 101) (21 nt) located at the Position 378-398 of the gene, Tm = 60°C

Antisense

- H1antisense

5' ACCTTCCTTGGTATCGTCTG 3' (SEQ ID NO: 102) (20 nt) located at the Position 722-741 of the gene, Tm = 60°C

- H2antisense

5' GAAACCAGCAGATGATGAACG 3' (SEQ ID NO: 103) (21 nt) located at the Position 722-742 of the gene, Tm = 62°C

- H3antisense

5' GCATCTGGTGGGGTTCTG 3' (SEQ ID NO: 104) (19 nt) located at the Position 722-740 of the gene, Tm = 62°C

Size of the amplified product ranges from 359 to 364 bp.

Appl. No. : 09/817,014
Filed : March 23, 2001

The following capture probes have been chosen for the specific capture of the histamine receptor sequences.

Capture probes

H1 5' CCCCAGGATGGTAGCGGA 3' (18 nt) (SEQ ID NO: 105)

H2 5' AGGATAGGGTGTAGAAATAAC 3' (22 nt) (SEQ ID NO: 106)

H3 5' TCTCGTGTCCCCCTGCTG 3' (18 nt) (SEQ ID NO: 107)

Each of the sequences above comprises a spacer at its 5' end

Spacer sequence 5' GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ ID NO: 36). Capture probes are aminated at their 5' end.

Example 12: Identification of G-protein serotonin receptors subtypes in rat

Serotonin Receptor coupled to the G-protein are all amplified with the following primers

Sense

- Consensus for the subtypes 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 4, 6, 7

5'ATC~~H~~TGCACCT~~S~~TGB~~G~~B~~C~~AT 3' (SEQ ID NO: 108) Tm = 58-64°C (20 nt)

H = C or A or T

S = C or G

B = C or T or G

1A ATCCTGCACCTGTGCGCCAT (0 mismatch) position 370-389 (SEQ ID NO: 109)

1B ATCATGCATCTCTGTGTCAT (1 mismatch) position 397-416 (SEQ ID NO: 110)

1C ATCATGCACCTCTGCGGCCAT (0 mismatch) position 427-446 (SEQ ID NO: 111)

1D ATCCTGCATCTCTGTGTCAT (1 mismatch) position 367-386 (SEQ ID NO: 112)

1E ATCTTGCACCTGTCGGCTAT (2 mismatch) position 331-350 (SEQ ID NO: 113)

2A ATCATGCACCTCTGCGCCAT (0 mismatch) position 487-506 (SEQ ID NO: 114)

2B ATCATGCATCTCTGTGCCAT (1 mismatch) position 424-443 (SEQ ID NO: 115)

2C ATCATGCACCTCTGCGCCAT (0 mismatch) position 24-43 (SEQ ID NO: 116)

4 ATTTTCACCTCTGCTGCAT (3 mismatchs) (SEQ ID NO: 117)

Appl. No. : 09/817,014
Filed : March 23, 2001

6 ATCCTAACCTCTGCTTCAT (3 mismatchs) (SEQ ID NO: 118)

7 ATCATGACCCTGTGCGTGAT (3 mismatchs) (SEQ ID NO: 119)

- Consensus 4, 6

5' ATCYTYCACCTCTGCYKCAT 3' (SEQ ID NO: 120) Tm = 52-64°C (20 nt)

K = G or T

Y = T or C

4 ATTTTCACCTCTGCTGCAT (SEQ ID NO: 121) (1 mismatch) position 322-341

6 ATTTTCACCTCTGCTGCAT (SEQ ID NO: 122) (1 mismatch) position 340-359

- Consensus 5A, 5B

5' ATCTGGAAYGTGRAGCCAT 3' (SEQ ID NO: 123) Tm = 58-62°C (20 nt)

Y = T or C

R = A or G

5A ATCTGGAATGTGACAGCAAT (SEQ ID NO: 124) (1 mismatch) position 385-404

5B ATCTGGAACGTGGCGGCCAT (SEQ ID NO: 125) (1 mismatch) position 424-443

- Specific 7

5' ATCATGACCCTGTGCGTGAT 3' (SEQ ID NO: 126) Tm = 56°C (18 nt) position 517-536

- Specific 3B

5' CTTCCGGAACGATTAGAAA 3' (SEQ ID NO: 127) Tm = 54°C (19 nt) position 404-422

Antisense

- Consensus for the subtypes 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 4, 7 Tm = 48-58 °C

5' TTGGHNGCYTTCYGBT 3' (SEQ ID NO: 128)

H = A or T or C

N = A or C or G or T

B = C or T or G

1A TTCACCGTCTCCTTC (4 mismatchs) (SEQ ID NO: 129)

Appl. No. : 09/817,014
Filed : March 23, 2001

1B TTGGTGGCTTGCGCTC (1 mismatch) position 913-929 (SEQ ID NO: 130)

1C TTGGAAGCTTCCTTTTC (1 mismatch) position 922-938 (SEQ ID NO: 131)

1D TTAGTGGCTTCCTTTC (2 mismatches) position 877-893 (SEQ ID NO: 132)

1E GTGGCTGCTTGCGTTC (2 mismatches) position 862-878 (SEQ ID NO: 133)

2A TTGCACGCCTTGCTC (2 mismatches) position 952-968 (SEQ ID NO: 134)

2B TTTGAGGCTCTGTTC (2 mismatches) position 952-968 (SEQ ID NO: 135)

2C TTGGAAGCTTCCTTTTC (1 mismatch) position 424-440 (SEQ ID NO: 136)

4 TTGGCTGCTTCGGTC (2 mismatches) (SEQ ID NO: 137)

7 GTGGCTGCTTCCTGTTC (1 mismatch) position 973-989 (SEQ ID NO: 138)

- Specific 1A

5' TTCACCGTCTTCCTTTC 3' (SEQ ID NO: 139) Tm = 50°C (17 nt) position 1018-1034

- Specific 4

5' TCTTGGCTGCTTGTC 3' (SEQ ID NO: 140) Tm = 52°C (17 nt) position 762-778

- Specific 6

5' ATAAAGAGCGGGTAGATG 3' (SEQ ID NO: 141) Tm = 52°C (18 nt) position 945-963

- Consensus 5A, 5B

5' CCTTCTGCTCCCTCCA 3' (SEQ ID NO: 142) Tm = 52°C (16 nt)

5A CCTTCTGTTCCCTCCA (1 mismatch) position 823-840 (SEQ ID NO: 143)

5B CCTTCTGCTCCCGCCA (1 mismatch) position 862-879 (SEQ ID NO: 144)

- Specific 3B

5' ACCGGGGACTCTGTGT 3' (SEQ ID NO: 145) Tm = 52°C (16 nt) position 1072-1089

The following capture probes have been chosen for the specific capture of the serotonin receptor subtypes sequences.

Appl. No. : 09/817,014
Filed : March 23, 2001

Capture probes

HTR1C 5' CTATGCTCAATAGGATTACGT 3' (21 nt) (SEQ ID NO: 146)
HTR2A 5' GTGGTGAATGGGGTTCTGG 3' (19 nt) (SEQ ID NO: 147)
HTR2B 5' TGGCCTGAATTGGCTTTGA 3' (21 nt) (SEQ ID NO: 148)
HTR2C/1C 5' TTATTCACGAACACTTGCTTT 3' (22 nt) (SEQ ID NO: 149)
HTR1B 5' AATAGTCCACCGCATCAGTG 3' (20 nt) (SEQ ID NO: 150)
HTR1D 5' GTACTCCAGGGCATCGGTG 3' (19 nt) (SEQ ID NO: 151)
HTR1A 5' CATACTCTATAGGGTCGGTG 3' (20 nt) (SEQ ID NO: 152)
HTR1E 5' ATACTCGACTGCGTCTGTGA 3' (20 nt) (SEQ ID NO: 153)
HTR7 5' GTACGTGAGGGGTCTCGTG 3' (19 nt) (SEQ ID NO: 154)
HTR5A 5' GGCGCGTTATTGACCAGTA 3' (19 nt) (SEQ ID NO: 155)
HTR5B 5' GGCGCGTGATAGTCCAGT 3' (18 nt) (SEQ ID NO: 156)
HTR3B 5' GATATCAAAGGGAAAGCGTA 3' (21 nt) (SEQ ID NO: 157)
HTR4 5' AAACCAAAGGTTGACAGCAG 3' (20 nt) (SEQ ID NO: 158)
HTR6 5' GTAGCGCAGCGCGAGAG 3' (18 nt) (SEQ ID NO: 159)

Each of the sequences above comprises a spacer at its 5' end

Spacer sequence 5' GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ ID NO: 36). Capture probes are aminated at their 5' end.

Example 13 : Identification of the HLA-A subtypes

The HLA-A subtypes are amplified with the following consensus primers

Sense

IPSCONA 5' GACAGCGACGCCGCGAGCCA 3' (SEQ ID NO: 160) located at the position 181-200 of the gene, Tm = 70°C

Antisense

IPASCONA 5 CGTGCCTGGTCTGGCCTCC 3' (SEQ ID NO: 161) located at the position 735-754 of the gene, Tm = 74°C

The size of the amplified product is 574 bp

Appl. No. : 09/817,014
Filed : March 23, 2001

The following capture probes of 27 nucleotides have been chosen for the specific capture of the HLA-A sequences

Capture probes

HLA-A1 ITSA01 5' GGAGGGCCGGTGCCTGGACGGGCTCCG 3' (SEQ ID NO: 162)
HLA-A2 ITASA02 5' TCTCCCCGTCCAATACTCCGGACCCT 3' (SEQ ID NO: 163)
HLA-A3 ITASA03A 5' CTGGGCCTTCACATTCCGTGTCTCCTG 3' (SEQ ID NO: 164)
ITSA03B 5' AGCGCAAGTGGGAGGCAGGCCATGAGG 3' (SEQ ID NO: 165)
HLA-A11 ITSA11A 5' GCCCATGCGCGGGAGCAGCAGAGAGCC 3' (SEQ ID NO: 166)
ITSA11B 5' CCTGGAGGGCCGGTGCCTGGAGTGGCT 3' (SEQ ID NO: 167)
HLA-A23 ITSA23A 5' GCCCGTGTGGCGGAGCAGTTGAGAGCC 3' (SEQ ID NO: 168)
ITASA23B 5' CCTTCACTTCCCTGTCTCCTCGTCCC 3' (SEQ ID NO: 169)
HLA-A24 ITSA24A 5' GCCCATGTGGCGGAGCAGCAGAGAGCC 3' (SEQ ID NO: 170)
ITASA24B 5' TAGCGGAGCGCGATCCGCAGGTTCTCT 3' (SEQ ID NO: 171)
HLA-A25 ITASA25A 5' TAGCGGAGCGCGATCCGCAGGCTCTCT 3' (SEQ ID NO: 172)
ITASA25B 5' TCACATTCCGTGTGTTCCGGTCCAAT 3' (SEQ ID NO: 173)
HLA-A26 ITASA26 5' GGGTCCCCAGGTTCGCTCGGTCACT 3' (SEQ ID NO: 174)
HLA-A29 ITASA29 5' TCACATTCCGTGTGCAGGTCCAAT 3' (SEQ ID NO: 175)
HLA-A30 ITASA30 5' CGTAGGCGTGCTGTTCATACCCGCGGA 3' (SEQ ID NO: 176)
HLA-A31 ITASA31 5' CCCAATACTCAGGCCTCTCCTGCTCTA 3' (SEQ ID NO: 177)
HLA-A33 ITSA33 5' CGCACGGACCCCCCCCAGGACGCATATG 3' (SEQ ID NO: 178)
HLA-A68 ITSA68A 5' GGCAGGCCATGTGGCGGAGCAGTGGAG 3' (SEQ ID NO: 179)
ITASA68B 5' GTCTAGGCGTCCTGCCGGTACCCGCG 3' (SEQ ID NO: 180)
HLA-A69 ITASA69 5' ATCCTCTGGACGGTGTGAGAACCGGCC 3' (SEQ ID NO: 181)

Appl. No. : 09/817,014
Filed : March 23, 2001

Each of the sequences above comprises an aminated spacer at its 5' end. Spacer sequence 5'
GAATTCAAAGTTGCTGAGAATAGTTCAATGGAAGGAAGCG 3' (SEQ ID NO: 36)

Example 14: Identification of Cytochrome P450 3a forms

The Cytochrome P450 forms are amplified with the following consensus primers

Sense

- Consensus
5' GCCAGAGCCTGAGGA 3' (SEQ ID NO: 182) located at the position 1297-1311 of the 3a3 gene, Tm = 50°C

Antisense

- Consensus a3, a23, a1, a2
5' TCAAAAGAAATTAACAGAGA 3' (SEQ ID NO: 183) located at the position 1839-1858 of the 3a3 gene, Tm = 50°C

- Specific a9
5' ACAATGAAGGTAACATAGG 3' (SEQ ID NO: 184) located at the position 2015-2033 of the 3a9 gene Tm = 52°C

- Specific a18
5' ACTGATGGAACTAACGG 3' (SEQ ID NO: 185) located at the position 1830-1846 of the 3a18 gene Tm = 52°C

The length of the PCR product is around 560 bp.

The following capture probes have been chosen for the specific capture of the cytochrome P-450 3a sequences.

Capture probe

3a1 5' TGTTTGATTGGTACATCTTG 3' (23 nt) (SEQ ID NO: 186)